naire designed to measure the severity of the disease were analysed to assess whether there was a difference between the treatment groups in terms of change in severity over the 6 month period. **METHODS:** Latent Transition Analysis is used to explain the responses to the questionnaire by grouping patients into categories (severity groups) based on their responses. There are three parameters that can be estimated using LTA; Membership probabilities (probability of belonging to a particular severity category); Transition probabilities (probability of moving to a particular severity category) and Item response probabilities. These parameters are compared between the two treatment groups to determine if there is a difference between them. Two covariates were included in the model to investigate their effects. **RESULTS:** The analysis showed that there was no significant difference between the treatment groups in terms of Membership probabilities or Transition probabilities. One of the covariates was found to have a significant effect on the responses. The effect of the covariate was different for the two treatment groups and had an opposite effect on the Placebo group compared the effect on the Active group. **CONCLUSIONS:** It has been shown that LTA can be a useful tool for analysing multivariate ordinal data and that its application in clinical data analysis has advantages over some of the more common techniques.

PRM151

COLLAPSIBILITY AND CENSORING: WHAT'S THE BIAS IN ESTIMATED SURVIVAL TIME?

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OBJECTIVES: Treatment effects in survival analysis are often expressed as hazard ratios (HR), which are not useful in cost-effectiveness analysis since they do not entail units of health. Fortunately, parametric survival models can also be used to estimate projected mean survival time (T). Two problems in survival analysis are often misunderstood or ignored: non-collapsibility and omitted-variable bias due to censoring. Non-collapsibility exists when the treatment effect changes as prognostic covariates are added to the regression model, even when confounding is absent (e.g. in a randomized controlled trial (RCT)). While HRs are known to be non-collapsible, it has not yet been demonstrated whether non-collapsibility affects T. Censoring induces bias when it is associated with patient characteristics and no adjustment is undertaken. The objectives of this study were to disentangle the effects of non-collapsibility and censoring bias and assess their impact on estimates of T. **METHODS:** Survival, treatment and five normally distributed prognostic covariates were simulated in RCT-like datasets with and without censoring. Weibull regression models with an increasing number of covariates were used to calculate the HR for treatment and T. **RESULTS:** For uncensored data, HRs decreased with the inclusion of additional covariates, while T remained constant. For the censored data, T increased sharply with the inclusion of additional covariates, while the HRs decreased. The estimates of the full model of both outcome measures were close to the means from the dataset, although the model was estimated on censored data. **CONCLUSIONS:** Analysis of the synthesized data makes it possible to distinguish between the impact of non-collapsibility and censoring on HR and T. While the HR is non-collapsible, T is collapsible. It can be used in cost-effectiveness analysis, as long as all important prognostic factors are included in the regression. The latter is a weakness of currently common analyses of RCT data.

RESEARCH ON METHODS - Study Design

PRM152

IS IT JUST SEMANTICS? THE USE OF "EFFICACY" AND "EFFECTIVENESS" IN COMPARATIVE EFFECTIVENESS REVIEWS AND HEALTH TECHNOLOGY ASSESSMENTS

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OBJECTIVES: To explore and quantify the extent to which the terms "efficacy" and "effectiveness" are used consistently and correctly in and Health Technology Assessments (HTAs). Efficacy describes a drug's effect in ideal and controlled circumstances (i.e. in clinical trials). Effectiveness describes the success of a drug in usual or "real world" practices in which all conditions cannot be controlled. Effectiveness is much more difficult to assess and is often measured by observational studies or calculated by a meta-analysis of clinical trial results. **METHODS:** We examined 38 HTAs published from 2005-2011 covering 13 disease conditions from 6 agencies (AHRQ, DERP, CADTH, IQWiG, NICE, and NHS Scotland), which included 115 pharmaceutical products. We categorized each HTA based on whether their stated main objective was to measure either clinical efficacy or clinical effectiveness. These stated main objectives were then compared to the evidence actually evaluated in the reported studies (ie. RCTs and/or observational studies). We quantified and analyzed discrepancies between the stated objectives and actual objectives. **RESULTS:** Of the 38 HTAs, 37 evaluated efficacy and 1 focused on effectiveness. Eighteen reviews (47%) described their main objective, efficacy or effectiveness, consistent with the actual evidence evaluated. Twenty reviews (53%) stated their main objective was measuring clinical effectiveness, but presented evidence assessing clinical efficacy. Of the 6 agencies, NICE and NHS Scotland showed the highest percentages of discrepancies between stated objectives and evidence evaluated (80% and 100% respectively), while AHRQ and DERP had the lowest (0% and 29% respectively). **CONCLUSIONS:** Though the distinction between "efficacy" and "effectiveness" is substantial, the terms are not always used appropriately or consistently. Often, the uses of the terms in HTAs are misleading. This is a barrier to clear communication, but the implications might be broader.

PRM153

PRIORITIZING MULTIPLE PATIENT-RELEVANT ENDPOINTS - A METHODOLOGICAL COMPARISON OF CONJOINT ANALYSIS AND ANALYTIC HIERARCHY PROCESS CONSIDERING IQWIG'S EFFICIENCY FRONTIER CONCEPT

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OBJECTIVES: The Institute for Quality and Efficiency in Health Care (IQWiG) in Germany evaluates benefits/harms and economic implications of medical interventions. For the purpose of cost-benefit analysis, IQWiG has developed the efficiency frontier concept to determine the maximum reimbursable price for pharmaceuticals. Within this concept benefits/harms are evaluated for each patient-relevant endpoint. Methodological problems arise with the presence of multiple patient-relevant endpoints because recommendations for the maximum reimbursable price will likely be imprecise. Conjoint analysis (CA) and analytic hierarchy process (AHP) are being discussed as potential approaches to aggregate multiple patient-relevant endpoints. The objective of this contribution was to describe both approaches and compare them with respect to their suitability as a method for aggregating multiple patient-relevant endpoints within IQWiG's efficiency frontier concept. **METHODS:** A catalogue with criteria has been established to assess both approaches with regard to their suitability for aggregating multiple patient-relevant endpoints. The catalogue comprises nine relevant legal and methodological aspects: two criteria were identified based on legal requirements; three criteria were included considering IQWiG method requirements; lastly, four general methodological requirements were considered. **RESULTS:** Both methods were assessed based on these criteria. Two criteria were identified that could be met by both CA and AHP. The remaining seven criteria could be met by either CA or AHP. None of IQWiG's proposed approaches for prioritizing and weighting multiple patient-relevant endpoints could demonstrate to fulfill all relevant criteria when assessed with regard to legal and methodological requirements. **CONCLUSIONS:** With the presence of multiple patient-relevant endpoints the implementation of the efficiency frontier concept remains unclear due to lack of methodological guidance on how to aggregate multiple endpoints. There is substantial need for further (empirical) research in methods for aggregating multiple patient-relevant endpoints.

PRM154

SOURCE DATA VERIFICATION – A SURVEY OF CURRENT PRACTICE

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OBJECTIVES: During the last few years, there has been an increasing trend towards more cost-effective monitoring of clinical trials and non-interventional studies. Cost efficiencies can by gained with partial source data verification (SDV). The impact of partial SDV on the accuracy of the data in these studies is unknown. In order to propose an optimal level and method of partial SDV, we first need a better understanding of the rates and types of discrepancies found while conducting SDV. **METHODS:** PPD CRAs in NA and EMEA were invited to participate in an on-line survey of 11 questions pertaining to level of SDV employed in studies and the quantity/type of discrepancies found. PRELIMINARY **RESULTS:** Current response rate to this survey is 28% (589/2094), with a completion rate of 83% (491/589). Only 26% (127/491) of the respondents report having used partial SDV, which was defined as anything less than 100% SDV ("I always verify all of the data"). When asked to estimate the average amount of discrepancy (all data fields) encountered between source data and CRF, two-thirds of the respondents report a typical burden of 20% or less. Not surprisingly, the most common data discrepancies involve the recoding of: concomitant medications (27%) followed by AEs and/or SAEs (20%). Of those respondents who had experience with partial SDV, 32% (41/127) reported an approach that combines 'all data points within a subset of CRFs' with 'selected data points in all CRFs'. When asked about their willingness to participate in a follow-up interview with more detailed questions about experiences with SDV, 33% (163/491) of the respondents answered 'yes'. **CONCLUSIONS:** The results of this survey and its planned follow-up survey will be helpful in evaluating optimal methods and levels of partial SDV in both clinical trials and observational studies.

PRM155

A PRAGMATIC RANDOMIZED CLINICAL TRIALS – DESIGN AND QUALITY ASSESSMENT OF THE SOURCE OF EFFECTIVENESS DATA

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OBJECTIVES: Acquisition of scientific data required for the rational decisions on health policy has became an important tool in determining the validity of the financing methods of treatment from public funds based on the health technology assessment (HTA). The primary source of scientific evidence for health technology assessment are randomized controlled trials (RCTs), because of their features (e.g. randomization or blindness) reducing methodological bias. These features may become a disadvantage, which markedly reduces the possibility of the transfer of the results and conclusions to the everyday practice. In this situation an important role begin to play pragmatic randomized controlled trials (PRCTs), providing highly reliable information about the effectiveness in contrast to observational studies or registries. However, an important problem is correct design and quality assessment of such trials. **METHODS:** A systematic review in Medline through Pubmed using the following queries: "(pragmatic OR practical OR naturalistic OR real world) AND (design OR quality)" was performed till June 2012 to gather and systematize the current information about pragmatic randomized trials to improve the quality of the practical effectiveness evaluation in health technology assessment reports. **RESULTS:** Using this search strategy nearly 28 000 hits were obtained. Preliminary